

FIGURE 1

A: BoNTA(H<sub>2</sub>) synthetic gene (Version #1) SEQ ID NO: 1

GAATTCGAAACGatCGTCTGCTGTCTACCTTCACTGAATACATCAAGAAC  
ATCATCAATACCTCCATCCTGAACCTGCGCTACGAATCCAATCACCTGAT  
CGACCTGTCTCGCTACGCTTCCAAAATCAACATCGGTTCTAAAGTAACT  
TCGATCCGATCGACAAGAATCAGATCCAGCTGTTCAATCTGGAATCTTCC  
AAAATCGAAGTTATCCTGAAGAATGCTATCGTATACAACCTCTATGTACG  
AAAACCTTCTCCACCTCCTTCTGGATCCGTATCCCGAAATACTTCAACTCC  
ATCTCTCTGAACAATGAATACACCATCATCAACTGCATGGAAAACAATT  
CTGGTTGGAAAGTATCTCTGAACCTACGGTGAAATCATCTGGACTCTGCAG  
GACACTCAGGAAATCAAACAGCGTGTGTATTCAAATACTCTCAGATGA  
TCAACATCTCTGACTACATCAATCGCTGGATCTTCGTTACCATCACCAAC  
AATCGTCTGAATAACTCCAAAATCTACATCAACGGCCGTCTGATCGACC  
AGAAACCGATCTCCAATCTGGGTAACATCCACGCTTCTAATAACATCATG  
TTCAAACCTGGACGGTTGTCGTGACACTACCGCTACATCTGGATCAAATA  
CTTCAATCTGTTTCGACAAAGAACTGAACGAAAAAGAAATCAAAGACCTG  
TACGACAACCAAGTCCAATTCTGGTATCCTGAAAGACTTCTGGGGTGACTA  
CCTGCAGTACGACAAACCGTACTACATGCTGAATCTGTACGATCCGAAC  
AAATACGTTGACGTCAACAATGTAGGTATCCGCGGTTACATGTACCTGA  
AAGGTCCGCGTGGTTCTGTTATGACTACCAACATCTACCTGAACTCTTCC  
CTGTACCGTGGTACCAAATTCATCATCAAGAAATACGCGTCTGGTAACA  
AGGACAATATCGTTCGCAACAATGATCGTGTATACATCAATGTTGTAGTT  
AAGAACAAGAATACCGTCTGGCTACCAATGCTTCTCAGGCTGGTGTAG  
AAAAGATCTTGTCTGCTCTGGAAATCCCGGACGTTGGTAATCTGTCTCAG  
GTAGTTGTAATGAAATCCAAGAACGACGAGGTATCACTAACAAATGCA  
AAATGAATCTGCAGGACAACAATGGTAACGATATCGGTTTCATCGGTTT  
CCACCAGTTCAACAATATCGCTAAACTGGTTGCTTCCAACTGGTACAATC  
GTCAGATCGAACGTTCTCTCGCACTCTGGGTTGCTCTTGGGAGTTCATC  
CCGTTGATGACGGTTGGGGTGAACGTCCGCTG<sub>taa</sub>GAATTC

B: BoNTA(H<sub>2</sub>) encoded protein (Version #1) SEQ ID NO: 2

MRLLSTFTEYIKNIINTSILNLRYESNHLIDLSRYASKINIGSKVNFDPIDKNQI  
QLFNLESSKIEVILKNAIVYNSMYENFSTSFWRIPKYFNSISLNNEYTIINCME  
NNSGWKVSLNYGEIWTLQDTQEIKQRVVFKYSQMINISDYINRWIFVTITNN  
RLNNSKIYINGRLIDQKPISNLGNIHASNNIMFKLDGCRDTHRYIWIKYFNLF  
DKELNEKEIKDLYDNQSNSGILKDFWGDYLQYDKPYMLNLYDPNKYVDV  
NNVGIRGYMYLKGPRGSVMTTNIYLNSSLYRGTKFIIKKYASGNKDNIVRN  
NDRVYINVVVKNKEYRLATNASQAGVEKILSALEIPDVGNLSQVVVMKSKN  
DQGITNKCKMNLQDNNNGNDIGFIGFHQFNNAKLVASNWNRYNIERSRRTL  
GCSWEFIPVDDGWGERPL\*

FIGURE 2

**A: BoNTA(H<sub>2</sub>) synthetic gene (version #2) SEQ ID NO: 3**

GAATTCGAAACGatgTCTACCTTCACTGAATACATCAAGAACATCATCAAT  
ACCTCCATCCTGAACCTGCGCTACGAATCCAATCACCTGATCGACCTGTC  
TCGCTACGCTTCCAAAATCAACATCGGTTCTAAAGTTAACTTCGATCCGA  
TCGACAAGAATCAGATCCAGCTGTTCAATCTGGAATCTTCCAAAATCGA  
AGTTATCCTGAAGAATGCTATCGTATACAACTCTATGTACGAAAATTCT  
CCACCTCCTTCTGGATCCGTATCCCGAAATACTTCAACTCCATCTCTCTG  
AACAATGAATACACCATCATCAACTGCATGGAAAACAATTCTGGTTGGA  
AAGTATCTCTGAACTACGGTGAAATCATCTGGACTCTGCAGGACACTCA  
GGAAATCAAACAGCGTGTTGTATTCAAATACTCTCAGATGATCAACATCT  
CTGACTACATCAATCGCTGGATCTTCGTTACCATCACCAACAATCGTCTG  
AATAACTCCAAAATCTACATCAACGGCCGTCTGATCGACCAGAAACCGA  
TCTCCAATCTGGGTAACATCCACGCTTCTAATAACATCATGTTCAAACCTG  
GACGGTTGTCGTGACACTCACCGCTACATCTGGATCAAATACTTCAATCT  
GTTTCGACAAAGAAGTGAACGAAAAAGAAATCAAAGACCTGTACGACAA  
CCAGTCCAATTCTGGTATCCTGAAAGACTTCTGGGGTGACTACCTGCAGT  
ACGACAAACCGTACTACATGCTGAATCTGTACGATCCGAACAAATACGT  
TGACGTCAACAATGTAGGTATCCGCGGTTACATGTACCTGAAAGGTCCG  
CGTGGTTCTGTTATGACTACCAACATCTACCTGAACTCTTCCCTGTACCG  
TGGTACCAAATTCATCATCAAGAAATACGCGTCTGGTAACAAGGACAAT  
ATCGTTCGCAACAATGATCGTGTATACATCAATGTTGTAGTTAAGAACAA  
AGAATACCGTCTGGCTACCAATGCTTCTCAGGCTGGTGTAGAAAAGATC  
TTGTCTGCTCTGGAAATCCCGGACGTTGGTAATCTGTCTCAGGTAGTTGT  
AATGAAATCCAAGAACGACCAGGGTATCACTAACAAATGCAAAATGAAT  
CTGCAGGACAACAATGGTAACGATATCGGTTTCATCGGTTTCCACCAGTT  
CAACAATATCGCTAAACTGGTTGCTTCCAACTGGTACAATCGTCAGATCG  
AACGTTCTCTCGCACTCTGGGTTGCTCTTGGGAGTTTCATCCCGGTTGAT  
GACGGTTGGGGTGAACGTCCGCTGtaaGAATTC

**B: BoNTA(H<sub>2</sub>) encoded protein (Version #2) SEQ ID NO: 4**

MSTFTEYIKNIINTSILNLRYESNHLIDLSRYASKINIGSKVNFDPIDKNQIQLF  
NLESSKIEVILKNAIVYNSMYENFSTSFWRIPKYFNSISLNNEYTIINCMENNS  
GWKVSILNYGEIHWTLQDTQEIKQRVVFYKYSQMINISDYINRWIFVTITNNRLN  
NSKIYINGRLIDQKPISNLGNIHASNNIMFKLDGCRDTHR YTWIKYFNLFDFKE  
LNEKEIKDLYDNQSNISGILKDFWGDYLYQYDKPYMYMLNLYDPNKYVDVNNV  
GIRGYMYLKGPRGSVMTTNIYLNSSLYRGTKFIKKYASGNKDNIVRNNDRV  
YINVVVKNKEYRLATNASQAGVEKILSALEIPDVGNLSQVVVMKSKNDQGI  
TNKCKMNLQDNNNGNDIGFIGFHQFNNAIKLVASNWYNRQIERSSRTLGCWSW  
EFIPVDDGWGERPL\*

FIGURE 3

A: BoNTA(H<sub>2</sub>) synthetic gene (Version #3) SEQ ID NO: 5

GAATTCGAAACGatgGCCTCTACCTTCACTGAATACATCAAGAACATCATC  
AATACCTCCATCCTGAACCTGCGCTACGAATCCAATCACCTGATCGACCT  
GTCTCGCTACGCTTCCAAAATCAACATCGGTTCTAAAGTTAACTTCGATC  
CGATCGACAAGAATCAGATCCAGCTGTTCAATCTGGAATCTTCCAAAAT  
CGAAGTTATCCTGAAGAATGCTATCGTATACAACTCTATGTACGAAAAC  
TCTCCACCTCCTTCTGGATCCGTATCCCGAAATACTTCAACTCCATCTCTC  
TGAACAATGAATACACCATCATCAACTGCATGGAAAACAATTCTGGTTG  
GAAAGTATCTCTGAACTACGGTGAAATCATCTGGACTCTGCAGGACACT  
CAGGAAATCAAACAGCGTGTTGTATTCAAATACTCTCAGATGATCAACA  
TCTCTGACTACATCAATCGCTGGATCTTCGTTACCATCACCAACAATCGT  
CTGAATAACTCCAAAATCTACATCAACGGCCGTCTGATCGACCAGAAAC  
CGATCTCCAATCTGGGTAAACATCCACGCTTCTAATAACATCATGTTCAA  
CTGGACGGTTGTCGTGACACTCACCGCTACATCTGGATCAAATACTTCAA  
TCTGTTTCGACAAAGAACTGAACGAAAAAGAAATCAAAGACCTGTACGAC  
AACCAGTCCAATTCTGGTATCCTGAAAGACTTCTGGGGTGACTACCTGCA  
GTACGACAAACCGTACTACATGCTGAATCTGTACGATCCGAACAAATAC  
GTTGACGTCAACAATGTAGGTATCCGCGGTTACATGTACCTGAAAGGTC  
CGCGTGGTTCTGTTATGACTACCAACATCTACCTGAACTCTTCCCTGTAC  
CGTGGTACCAAATTCATCATCAAGAAATACGCGTCTGGTAACAAGGACA  
ATATCGTTCGCAACAATGATCGTGTATACATCAATGTTGTAGTTAAGAAC  
AAAGAATACCGTCTGGCTACCAATGCTTCTCAGGCTGGTGTAGAAAAGA  
TCTTGTCTGCTCTGGAAATCCCGGACGTTGGTAATCTGTCTCAGGTAGTT  
GTAATGAAATCCAAGAACGACCAGGGTATCACTAACAAATGCAAAATGA  
ATCTGCAGGACAACAATGGTAACGATATCGGTTTCATCGGTTTCCACCAG  
TTCAACAATATCGCTAAACTGGTTGCTTCCAACCTGGTACAATCGTCAGAT  
CGAACGTTTCTCTCGCACTCTGGGTTGCTCTTGGGAGTTCATCCCGGTTG  
ATGACGGTTGGGGTGAACGTCCGCTGtaaGAATTC

B: BoNTA(H<sub>2</sub>) encoded protein (Version #3) SEQ ID NO: 6

MASTFTEYIKNIINTSILNLRYESNHLIDLSRYASKINIGSKVNFDPIDKNQIQL  
FNLESSKIEVILKNAIVYNSMYENFSTSFWRIPKYFNSISLNNEYTIINCMENN  
SGWKVSLNYGEIHWTLQDTQEIQRVVFKYSQMINISDYINRWIFVTITNNRL  
NNSKIYINGRLIDQKPISNLGNIHASNNIMFKLDGCRDTHRYIWIKYFNLFDK  
ELNEKEIKDLYDNQSNNGILKDFWGDYLYQYDKPYMNLNLYDPNKYVDVNN  
VGIRGYMYLKGRGSVMTTNIYLNSSLYRGTKFIKKYASGNKDNIVRNDR  
VYINVVVKNEYRLATNASQAGVEKILSALEIPDVGNLSQVVVMKSKNDQ  
GITNKCKMNLQDNNNGNDIGFIGFHQFNNAKLVASNWNRYNIERSSRTLGCSS  
WEFIPVDDGWGERPL\*

FIGURE 4

A: BoNTB(H<sub>c</sub>) synthetic gene SEQ ID NO: 7

GAATTCACGatGCCAACAAATACAATTCCGAAATCCTGAACAATATCAT  
CCTGAACCTGCGTTACAAAGACAACAATCTGATCGATCTGTCTGGTTACG  
GTGCTAAAGTTGAAGTATACGACGGTGTGAACTGAATGACAAGAACCA  
GTTCAAACCTGACCTCTTCCGCTAACTCTAAGATCCGTGTTACTCAGAATC  
AGAACATCATCTTCAACTCCGTATTCTCTGGACTTCTCTGTTTCCTTCTGGA  
TTCGTATCCCGAAATACAAGAACGACGGTATCCAGAATTACATCCACAA  
TGAATACACCATCATCAACTGCATGAAGAATAACTCTGGTTGGAAGATC  
TCCATCCGCGGTAACCGTATCATCTGGACTCTGATCGATATCAACGGTAA  
GACCAAATCTGTATTCTTTCGAATACAACATCCGTGAAGACATCTCTGAAT  
ACATCAATCGCTGGTTCTTCGTTACCATCACCAATAACCTGAACAATGCT  
AAAATCTACATCAACGGTAAACTGGAATCTAATACCGACATCAAAGACA  
TCCGTGAAGTTATCGCTAACGGTGAAATCATCTTCAAACCTGGACGGTGA  
CATCGATCGTACCCAGTTCATCTGGATGAAATACTTCTCCATCTTCAACA  
CCGAACCTGTCTCAGTCCAATATCGAAGAACGGTACAAGATCCAGTCTTA  
CTCCGAATACCTGAAAGACTTCTGGGGTAATCCGCTGATGTACAACAAA  
GAATACTATATGTTCAATGCTGGTAACAAGAACTCTTACATCAAACCTGA  
AGAAAGACTCTCCGGTTGGTGAAATCCTGACTCGTTCCAAATACAACCA  
GAACTCTAAATACATCAACTACCGCGACCTGTACATCGGTGAAAAGTTC  
ATCATCCGTCGCAAATCTAACTCTCAGTCCATCAATGATGACATCGTACG  
TAAAGAAGACTACATCTACCTGGACTTCTTCAACCTGAATCAGGAATGG  
CGTGTATACACCTACAAGTACTTCAAGAAAGAAGAAAAGCTTTTCC  
TGGCTCCGATCTCTGATTCCGACGAACTCTACAACACCATCCAGATCAAA  
GAATACGACGAACAGCCGACCTACTCTTGCCAGCTGCTGTTCAAGAAAG  
ATGAAGAATCTACTGACGAAATCGGTCTGATCGGTATCCACCGTTTCTAC  
GAATCTGGTATCGTATTCGAAGAATACAAGAACTACTTCTGCATCTCCAA  
ATGGTACCTGAAGGAAGTTAAACGCAAACCGTACAACCTGAAACTGGGT  
TGCAATTGGCAGTTCATCCCGAAAGACGAAGGTTGGACCGAAtagtaaGAA  
TTC

B: BoNTB(H<sub>c</sub>) encoded protein SEQ ID NO: 8

MANKYNSEILNNIILNLR YKDNNDLIDLSGYGAKVEVYDGVELNDKNQFKLT  
SSANSKIRVTQNQNIIFNSVFLDFSVSFWIRIPKYKNDGIQNYIHNEYTIINCM  
KNNSGWKISIRGNRIIWTLLIDINGKTKSVFFEYNIREDISEYINR WFFVTITNNL  
NNAKIYINGKLESNTDIKDIREVIANGEIIFKLDGDIDRTQFIWMKYFSIFNTEL  
SQSNIEERYKIQSYSEYLKDFWGNPLMYNKEYYMFNAGNKNSYIKLKKDSP  
VGEILTRSKYNQNSKYINYRDLYIGEKFIIIRKSNSQSINDDIVRKEDYIYLD  
FNLNQEW RVYTYKYFKKEEEKLFLAPISDSDELYNTIQIKEYDEQPTYSCQL  
LFFKDEESTDEIGLIGHRFYESGIVFEEYKDYFCISKWYLKEVKRKPYNLKL  
GCNWQFIPKDEGWTE\*\*

FIGURE 5

A: BoNTC<sub>1</sub>(H<sub>c</sub>) synthetic gene SEQ ID NO: 9

GAATTCACGatgACCATCCCATTCAACATCTTCTCCTACACCAACAACTCC  
CTGTTGAAGGACATCATCAACGAGTACTTCAACAACATCAACGACTCCA  
AGATCCTGTCCCTGCAGAACCGTAAGAACACCTTGGTCGACACCTCCGG  
TTACAACGCCGAGGTCTCCGAGGAGGGTGACGTCCAGCTGAACCCAATC  
TTCCCATTGCGACTTCAAGCTGGGTTCCTCCGGTGAGGACAGAGGTAAGGT  
CATCGTCACCCAGAACGAGAACATCGTCTACAACTCCATGTACGAGTCC  
TTCTCCATCTCCTTCTGGATCAGAATCAACAAGTGGGTCTCCAACCTGCC  
AGGTTACACCATCATCGACTCCGTCAAGAACAACCTCCGGTTGGTCCATCG  
GTATCATCTCCAACCTTCTGGTCTTCAACCTGAAGCAGAACGAGGACTCC  
GAGCAGTCCATCAACTTCTCCTACGACATCTCCAACAACGCTCCTGGTTA  
CAACAAGTGGTTCTTCGTCACCGTCACCAACAACATGATGGGTAACATG  
AAGATCTACATCAACGGTAAGCTGATCGACACCATCAAGGTCAAGGAGT  
TGACCGGTATCAACTTCTCCAAGACCATCACCTTCGAGATCAACAAGATC  
CCAGACACCGGTCTGATCACCTCCGACTCCGACAACATCAACATGTGGA  
TCCGTGACTTCTACATCTTCGCCAAGGAGTTGGACGGTAAGGACATCAA  
CATCCTGTTCAACTCCTTGCAGTACACCAACGTCGTCAAGGACTACTGGG  
GTAACGACCTGAGATAACAAGGAGTACTACATGGTCAACATCGACTA  
CTTGAACAGATACATGTACGCCAACTCCAGACAGATCGTCTTCAACACC  
AGACGTAACAACAACGACTTCAACGAGGGTTACAAGATCATCATCAAGC  
GTATCAGAGGTAACACCAACGACACCAGAGTCAGAGGTGGTGACATCCT  
GTACTTCGACATGACTATCAACAACAAGGCCTACAACCTGTTTCATGAAG  
AACGAGACCATGTACGCCGACAACCACTCCACCGAGGACATCTACGCCA  
TCGGTCTGCGTGAGCAGACCAAGGACATCAACGACAACATCATCTTCCA  
GATCCAGCCAATGAACAACACTTACTACTACGCTTCCCAGATCTTCAAGT  
CCAACCTCAACGGTGAGAACATCTCCGGTATCTGTTCCATCGGTACCTAC  
AGATTCCGTCTGGGTGGTGACTGGTACAGACACAACCTTGGTTCCAAC  
TGTCAAGCAGGGTAACTACGCCTCCTTGCTGGAGTCCACTTCCACCCACT  
GGGGATTCTGTCCTCCAGTCTCCGAGtaatagGAATTC

B: BoNTC<sub>1</sub>(H<sub>c</sub>) encoded protein SEQ ID NO: 10

MTIPFNIFS YTNNSLLKDIINEYFNNINDSKILSLQNRKNTLVDTSGYNAEVSE  
EGDVQLNPIFPDFKLGSSGEDRGKVIVTQENENIVYNSMYESFSISFWIRINK  
WVSNLPGYTIIDSVKNNSGWSIGHSNFLVFTLKQNEDEQSINFSYDISNNAP  
GYNKWFFVTVTNMMGMNMKIYINGKLIDTIKVKELTGINFSTITFEINKIPD  
TGLITSDSDNINMWIRDFYIFAKELDGKDINILFNSLQYTNVVKDYWGNDLR  
YNKEYYMVNIDYLNRYMYANSRQIVFNTRNNNDFNEG YKIIKRIRGNTN  
DTRVRGGDILYFDMTINNKA YNLFMKNETMYADNHSTEDIYAIGLREQTKD  
INDNII FQIQPMNNTYYYASQIFKSNFNGENISGICSIGTYRFRLGGDWYRHN  
YLVPTVKQGN YASLLESTSTHWGFVPVSE\*\*

FIGURE 6

A: BoNTD(H<sub>2</sub>) synthetic gene SEQ ID NO: 11

GAATTCACGatgCGTTTGAAGGCTAAGGTCAACGAGTCCTTCGAGAACAC  
CATGCCATTCAACATCTTCTCCTACACCAACAACCTCCTTGTTGAAGGACA  
TCATCAACGAGTACTTCAACTCCATCAACGACTCCAAGATCTTGTCCTTG  
CAGAACAAGAAGAACGCCTTGGTCGACACCTCCGGTTACAACGCCGAGG  
TCAGAGTCGGTGACAACGTCCAGTTGAACACCATCTACACCAACGACTT  
CAAGTTGTCTCTTCCGGTGACAAGATCATCGTCAACTTGAACAACAACA  
TCTTGTACTCCGCCATCTACGAGAACTCCTCTGTCTCCTTCTGGATCAAG  
ATCTCCAAGGACTTGACCAACTCCCACAACGAGTACACCATCATCAACT  
CCATCGAGCAGAACTCCGGTTGGAAGTTGTGTATCCGTAACGGTAACAT  
CGAGTGGATCTTGACAGGACGTCAACCGTAAGTACAAGTCCTTGATCTTCG  
ACTACTCCGAGTCCTTGTCCCACACCGGTTACACCAACAAGTGGTTCTTC  
GTCACCATCACCAACAACATCATGGGTTACATGAAGTTGTACATCAACG  
GTGAGTTGAAGCAGTCCCAGAAGATCGAGGACCTGGACGAGGTCAAGCT  
GGACAAGACCATCGTCTTTCGGTATCGACGAGAACATCGACGAGAACCAG  
ATGTTGTGGATCCGTGACTTCAACATCTTCTCCAAGGAGCTGTCCAACGA  
GGACATCAACATCGTCTACGAGGGTCAGATCCTGAGGAACGTCATCAAG  
GACTACTGGGGTAACCCACTGAAGTTCGACACCGAGTACTACATCATCA  
ACGACAACATACATCGACCGTTACATCGCCCCAGAGTCCAACGTCCTGGT  
CCTGGTCCAGTACCCTGACCGTTCCAAGCTGTACACCGGTAACCCATCA  
CCATCAAGTCCGTCTCCGACAAGAACCCTTACTCCCGTATCCTGAACGGT  
GACAACATCATCCTGCACATGCTGTACAACTCCCGTAAGTACATGATCAT  
CCGTGACACCGACACCATCTACGCCACCCAGGGTGGTGACTGTTCCCAG  
AACTGTGTCTACGCCCTGAAGCTGCAGTCCAACCTGGGTAACCTACGGTAT  
CGGTATCTTCTCCATCAAGAACATCGTCTCCAAGAACAAGTACTGCTCCC  
AGATCTTCTCCTCCTTCCGTGAGAACACCATGCTGCTGGCCGACATCTAC  
AAGCCTTGGCGTTTCTCCTTCAAGAACGCCTACACTCCTGTGCGCGTCAC  
CAACTACGAGACCAAGCTGCTGTCCACCTCCTCCTTCTGGAAGTTCATCT  
CCCGTGACCCAGGTTGGGTCGAGtaatagGAATTC

B: BoNTD(H<sub>2</sub>) encoded protein SEQ ID NO: 12

MRLKAKVNESFENTMPFNIFS YTNNSLLKDIINEYFNSINDSKILSLQNKKNA  
LVDTSGYNAEVRVGDNVQLNTIYTNDFKLSSSGDKIIVNLNNNLYSAIYENS  
SVSFWIKISKDLTNSHNEYTIINSIEQNSGWKLCIRNGNIEWILQDVNRKYKS  
LIFDYSESLSHTGYTNKWWFVTITNNIMGYMKLYINGELKQSQKIEDLDEVK  
LDKTIVFGIDENIDENQMLWIRDFNIFSKELSNEDINIVYEGQILRNVIKDYW  
GNPLKFDTEYYIINDNYIDRYIAPESNVLVLVQYPDRSKLYTGNPITIKSVSD  
KNPYSRILNGDNILHMLYNSRKYMIIRD TDTIYATQGGDCSQNCVYALKLQ  
SNLGNYGIGIFS IKNIVSKNKYCSQIFSSFRENTMLLADIYKPWRFSFKNAYTP  
VAVTNYETKLLSTSSFWKFI SRDPGWVE\*\*

FIGURE 7

**A: BoNTE(H<sub>2</sub>) synthetic gene SEQ ID NO: 13**

GAATTCACCatgGGAGAGAGTCAGCAAGAACTAAATTCTATGGTAACTGA  
TACCCTAAATAATAGTATTCCTTTTAAGCTTTCTTCTTATACAGATGATAA  
AATTTTAATTTCTACTTCAACAAGTTCTTCAAGAGAATTAAGTCTTCTTC  
CGTTTTAAACATGAGATACAAGAATGATAAATACGTCGACACTTCCGGT  
TACGACTCCAATATCAACATTAACGGTGACGTGTACAAGTACCCAATA  
ACAAAAACCAATTCGGTATCTACAACGACAAGCTTACTGAGCTGAACAT  
CTCTCAAAACGACTACATTATCTACGACAACAAGTACAAGAAGTCTCTTA  
TTTCTTTCTGGGTCAGGATTCCTAACTACGACAACAAGATCGTCAACGTT  
AACACGAGTACACTATCATCAACTGTATGAGAGACAACAAGTCCGGT  
GGAAGGTCTCTCTTAACCACAACGAGATCATTTGGACCTTGCAAGACAA  
CGCAGGTATTAACCAAAAGTTAGCATTCAACTACGGTAACGCAAACGGT  
ATTTCTGACTACATCAACAAGTGGATTTTCGTCCTACTACTAACGACAG  
ATTAGGTGACTCTAAGCTTTACATTAACGGTAACTTAATCGACCAAAAGT  
CCATTTTAACTTAGGTAACATTACGTTTCTGACAACATCTTATTCAAG  
ATCGTTAACTGCAGTTACACCAGATACATTGGCATTAGATACTTCAACAT  
TTTCGACAAGGAGTTAGACGAGACCGAGATTCAAACCTTTATACAGCAAC  
GAACCTAACACCAATATTTTGAAGGACTTCTGGGGTAACTACTTGCTTTA  
CGACAAGGAATACTACTTATTAACGTGTTAAAGCCAAACAAGTTCATT  
GATAGGAGAAAGGATTCTACTTTAAGCATTAAACAACATCAGAAGCACTA  
TTCTTTTAGCTAACAGATTATACTCTGGTATCAAGGTTAAGATCCAAAGA  
GTTAACAAGTCTTCTACTAACGATAACCTTGTTAGAAAGAACGATCAGGT  
CTATATTAAGTTCGTCGCTAGCAAGACTCACTTATTCCCATTATATGCTG  
ATACCGCTACCACCAACAAGGAGAAGACCATCAAGATCTCCTCCTCTGG  
CAACAGATTTAACCAAGTCGTCGTTATGAACTCCGTCGGTAAACAAGTGA  
CCATGAACTTTAAAAATAATAATGGAAATAATATTGGGTTGTTAGGTTTC  
AAGGCAGATACTGTAGTTGCTAGTACTTGGTATTATACCCACATGAGAG  
ATCACACCAACAGCAATGGATGTTTTTGGAACTTTATTTCTGAAGAACAT  
GGATGGCAAGAAAAAataa

TagGGATCC GCGGCCGC ACGCGT CCCGGG ACTAGT GAATTC

**B: BoNTE(H<sub>2</sub>) encoded protein SEQ ID NO: 14**

MGESQQELNSMVTDTLNNISIPFKLSSYTDDKILISYFNKFFKRIKSSSVLNMR  
YKNDKYVDTSYDSNININGDVYKYPTNKNQFGIYNDKLTENISQNDYIIY  
DNKYKNFSISFWVRIPNYDNKIVNVNNEYTIINCMRDNNNGWKVSLNHNEII  
WTLQDNAGINQKLAFFNYGNANGISDYINKWIFVTITNDRLGDSKLYINGNLI  
DQKSILNLGNIHVSDNILFKIVNCSYTRYIGIRYFNIFDKELDETEIQTLYSNEP  
NTNLIKDFWGNLYLLYDKEYLLNLVLPNNFIDRRKDSTLSINNIRSTILLANR  
LYSGIKVKIQRVNNSSTNDNLVRKNDQVYINFVASKTHLFLYADTATTNKE  
KTIKISSSGNRNFNQVVMNSVGNCTMNFKNNGNNGNIGLLGFKADTVVAST  
WYYTHMRDHTNSNGCFWNFISEEHGWQEK\*\*

Enclume 1

100220" 58101660

AMINO ACID AND DESIGNED NUCLEOTIDE SEQUENCE OF BONTE(Hc)

Asu II  
TTC GAA ACC ATG ATT TTA ATT TCC TAC TTC AAC AAG TTC TTC AAG AGA ATT AAG TCT TCC GTT TTA AAC ATG AGA TAC AAG AAT GAT AAA TAC GTC  
M I L I S Y F N K F F K R I K S S S V L N M R Y K N D K Y V  
GAC ACT TCC GGT TAC GAC TCC AAT ATC AAC ATT AAC GGT GAC GTG TAC AAG TAC CCA ACT AAC AAA AAC CAA TTC GGT ATC TAC AAC GAC AAG CTT ACT GAG CTG  
D T S G Y D S N I N I N G D V Y K Y P T N K N Q F G I Y N D K L (T) E L  
AAC ATC TCT CAA AAC GAC TAC ATT ATC TAC GAC AAC AAG TAC AAG AAC TTC TCT ATT TCT TTC TGG GTC AGA ATT CCA TAC GAC AAC AAG ATC GTC AAC GTT  
N I S Q N D Y I I Y D N K Y K N F S I S F W V R I P N Y D N K I V N V  
AAC AAC GAG TAC ACT ATC AAC TGT ATG AGA GAC AAC AAC TCC GGT TGG AAG GTC TCT CTT AAC CAC AAC GAG ATC ATT TGG ACC TTG CAA GAC AAC GCA GGT  
N N E Y T I I N C M R D N N S G W K V S L N H N E I I W (T) L Q D N A G  
ATT AAC CAA AAG TTA CCA TTC AAC TAC GGT AAC GCA AAC GGT ATT TCT GAC TAC ATC AAC AAG TGG ATT TTC GTC ACT ATC AAC GAC AGA TTA GGT GAC TCT  
I N Q K L A F N Y G N A N G I S D Y I N K W I F V T I T N D R L G D S  
AAG CTT TAC ATT AAC GGT AAC TTA ATC GAC CAA AAG TCC ATT TTA AAC TTA GGT AAC ATT CAC GTT TCT GAC AAC ATC TTA TTC AAG ATC GTT AAC TGC AGT TAC  
K L Y I N G N L I D Q K S I L N L G N I H V S D N I L F K I V N C S Y  
ACC AGA TAC ATT GGC ATT AGA TAC TTC AAC ATT TTC GAC AAG GAG TTA GAC GAG ACC GAG ATT CAA ACT TTA TAC AGC AAC GAA CCT AAC ACC AAT ATT TTG AAG  
T R Y I G I R Y F N I F D K E L D E T E I Q T L Y S N E P N T N I L K  
GAC TTC TGG GGT AAC TAC TTG CTT TAC GAC AAC GAA TAC TAC TTA AAC GTG TTA AAC CCA AAC AAC TTC ATT GAT AGG AGA AAG GAT TCT ACT TTA AGC ATT  
D F W G N Y L L Y D K E Y Y L L N V L K P N N F I D R R K D S T L S I  
AAC AAC ATC AGA ACC ACT ATT CTT TTA CCA AAC AGA TTA TAC TCT GGT ATC AAG GTT AAG ATC CAA AGA GTT AAC AAC TCT TCT ACT AAC GAT AAC CTT GTT AGA  
N N I R S T I L L A N R L Y S G I K V K I Q R V N N S S T N D N L V R  
AAG AAC GAT CAG GTC TAT ATT AAC TTC GTC GGT ACC AAG ACT CAC TTA TTC CCA TTA TAT GGT GAT ACC GGT ACC AAC AAG GAG AAG ACC ATC AAG ATC TCC  
K N D Q V Y I N F V A S K T H L F P L Y A D T A T T N K E K T I K I S  
TCC TCT GGC AAC AGA TTT AAC CAA GTC GTC GTT ATG AAC TCC GTC GGT AAC AAC TGT ACC ATG AAC TTT AAA AAT AAT AAT AAT ATT GGG TTG TTA GGT  
S S G N R F N Q V V M N S V G N N C T M N F K N N G N N I G L L G  
TTC AAG GCA GAT ACT GTA GTT GGT GGT AGT ACT TGG TAT TAT ACC CAC ATG AGA GAT CAC ACC AAC AGC AAT CGA TGT TTT TGG AAC TTT ATT TCT GAA GAA CAT GGA  
F K A D T V V A S  
TGG CAA GAA AAA TAA TAG CGA TCC  
W Q E K ter ter BamH I

Fig 8



FIGURE 9

A: BoNTF(H<sub>c</sub>) synthetic gene SEQ ID NO: 15

GAATTCACGatgTCCTACACCAACGACAAGATCCTGATCTTGTACTTCAAC  
AAGCTGTACAAGAAGATCAAGGACAACCTCCATCTTGGACATGAGATACG  
AAAACAATAAGTTCATCGACATCTCCGGTTACGGTTCCAACATCTCCATC  
AACGGTGACGTCTACATCTACTCCACCAATAGAAACCAGTTCGGAATCT  
ACTCCTCCAAGCCTTCCGAGGTCAACATCGCTCAGAACAAACGACATCAT  
CTACAACGGAAGATACCAGAACTTCTCCATCTCCTTCTGGGTCCGTATCC  
CAAAGTACTTCAACAAGGTCAACCTGAATAACGAGTACACCATCATCGA  
CTGCATCCGTAACAATAACTCCGGATGGAAGATCTCCCTGAACTACAAC  
AAGATCATCTGGACCCTGCAGGACACCGCCGGTAACAATCAGAAGTTGG  
TCTTCAACTACACCCAGATGATCTCCATCTCCGACTACATCAACAAGTGG  
ATCTTCGTCACCATCACCAATAACCGTTTGGGAAACTCCAGAATCTACAT  
CAACGGTAACTTGATCGACGAGAAGTCCATCTCCAACCTTGGGTGACATC  
CACGTCTCCGACAACATTTTGTTCAGATCGTCGGTTGTAACGACACCCG  
TTACGTCGGGATCCGTTACTTCAAAGTCTTCGACACTGAGTTGGGTAAAG  
CCGAGATCGAGACCTTGTACTCCGACGAGCCTGACCCATCCATCCTGAA  
GGACTTCTGGGGTAACTACCTGCTGTACAACAAACGTTACTACTTGCTGA  
ACTTGTTGCGTACCGACAAGTCCATCACCCAGAACTCCAACCTTCTTGAAC  
ATCAACCAGCAGAGAGGTGTCTACCAGAAGCCAAACATCTTCTCCAACA  
CCAGATTGTACACCGGAGTCGAGGTCAATTATCAGAAAGAACGGATCTAC  
TGATATTTCCAACACCGATAACTTCGTCAGAAAGAACGATCTGGCTTACA  
TCAACGTTGTCGACAGAGATGTCGAATACCGTCTGTACGCCGATATCTCT  
ATCGCCAAACCTGAAAAGATCATCAAGCTGATCCGTACCTCTAACTCTA  
ACAACTCTCTGGGACAAATCATCGTCATGGACTCCATCGGTAATAACTGT  
ACCATGAACTTCCAGAACAACAACGGTGGAAACATCGGTTTGTGGGT  
TCCACTCCAACAACTTGGTCGCTTCTCCTGGTACTACAACAACATCCGT  
AAGAACACCTCCTCCAACGGTTGCTTCTGGTCCTTCATCTCCAAGGAGCA  
CGGTTGGCAGGAGAACTaatagGAATTC

B: BoNTF(H<sub>c</sub>) encoded protein SEQ ID NO: 16

MSYTNDKILILYFNKLYKKIKDNSILDMRYENNKFIDISGYGSNISINGDVYIY  
STNRNQFGIYSSKPSEVNIAQNNDIYNGRYQNFSISFWVRIPKYFNKVNLNN  
EYTIIDCIRNNNSGWKISLNYNKIIWTLQDTAGNNQKLVFNYTQMISISDYIN  
KWIFVTITNNRLGNSRIYINGNLIDEKSISNLGDIHVSDNILFKIVGCNDTRYV  
GIRYFKVFDTELKGKTEIETLYSDEPDPSILKDFWGNLYLLYNKRYLLNLLRT  
DKSITQNSNFLNINQQRGVYQKPNIFSNTRLYTGVEVIIRKNGSTDISNTDNF  
VRKNDLAYINVVDRDVEYRLYADISIAKPEKIIKLRTSNSNNSLGQIIVMDSI  
GNNCTMNFQNNNGGNIGLLGFHSNNLVASSWYYNNIRKNTSSNGCFWSFIS  
KEHGWQEN\*\*

FIGURE 10

**A: BoNTG(H<sub>c</sub>) synthetic gene SEQ ID NO: 17**

GAATTCACGatgAAGGACACCATCCTGATCCAGGTCTTCAACAACTACATC  
TCCAACATCTCCTCCAACGCCATCCTGTCCCTGTCCTACCGTGGTGGTCG  
TCTGATCGACTCCTCCGGTTACGGAGCCACCATGAACGTCGGTTCGACG  
TCATCTTCAACGACATCGGTAACGGTCAGTTCAAGCTGAACAACTCCGA  
GAACTCCAACATCACCGCCCACCAAGTTCGTCGTCTACGACTCCA  
TGTTTCGACAACTTCTCCATCAACTTCTGGGTCCGTACCCCAAAGTACAAC  
AACAACGACATCCAGACCTACCTGCAGAACGAGTACACCATCATCTCCT  
GTATCAAGAACGACTCCGGTTGGAAGGTCTCCATCAAGGGAAACCGTAT  
CATCTGGACCCTGATCGACGTCAACGCCAAGTCCAAGTCCATCTTCTTCG  
AGTACTCCATCAAGGACAACATCTCCGACTACATCAACAAGTGGTTCTCC  
ATCACCATCACCAACGACCGTCTGGGTAACGCCAACATCTACATCAACG  
GTTCCCTGAAGAAGTCCGAGAAGATCCTGAACCTGGACCGTATCAACTC  
CTCCAACGACATCGACTTCAAGCTGATCAACTGTACCGACACCACCAAG  
TTCGTCTGGATCAAGGACTTCAACATCTTCGGTCGTGAGCTGAACGCCAC  
CGAGGTCTCCTCCCTGTACTGGATCCAGTCCTCCACCAACACCCTGAAGG  
ACTTCTGGGGAAACCCACTGCGTTACGACACCCAGTACTACCTGTTCAAC  
CAGGGTATGCAGAACATCTACATCAAGTACTTCTCCAAGGCCTCCATGG  
GTGAGACCGCCCCTCGTACCAACTTCAACAACGCCGCCATCAACTACCA  
GAACCTGTACCTGGGTCTGCGTTTCATCATCAAGAAGGCCTCCAACTCCC  
GTAACATCAACAACGACAACATCGTCCGTGAGGGTGACTACATCTACCT  
GAACATCGACAACATCTCCGACGAGTCCTACCGTGTCTACGTCCTGGTCA  
ACTCCAAGGAGATCCAGACCCAGCTGTTCTGGCCCCAATCAACGACGA  
CCCTACCTTCTACGACGTCCTGCAGATCAAGAAGTACTACGAGAAGACC  
ACCTACAACGTGTCAGATCCTGTGCGAGAAGGACACCAAGACCTTCGGAC  
TGTTCCGGTATCGGTAAGTTCGTCAAGGACTACGGTTACGTCTGGGACACC  
TACGACAACACTTCTGTATCTCCAGTGGTACCTGCGTCGTATCTCCGA  
GAACATCAACAAGCTGCGTCTGGGATGTAAGTGGCAGTTCATCCCAGTC  
GACGAGGGTTGGACCGAGGtaatagGAATTC

**B: BoNTG(H<sub>c</sub>) encoded protein SEQ ID NO: 18**

MKDILIQVFNNYISNISSNAILSLSYRGGRLIDSSGYGATMNVGSDVIFNDIG  
NGQFKLNSENSENITAHQSKFVVYDSMFDNFSINFWVRTPKYNNNDIQTYL  
QNEYTHISCIKND SGWKVSIKGNRIIWLIDVNAKSKSIFFEYSIKDNISDYINK  
WFSITITNDRLGNANIYINGSLKKSEKILNLDRLNSSNDIDFKLINCTDITKFKV  
WIKDFNIFGRELNATEVSSLYWIQSSTNTLKDFWGNPLRYDTQYYLFNQGM  
QNIYIKYFSKASMGETAPRTNFNNAAINYQNLYLGLRFIIKKASNSRNINNDN  
IVREGDYIYLNIDNISDESYRVYVLVNSKEIQTLFLAPINDDPTFYDVLQIKK  
YYEKTYYNCQILCEKDTKTFGLFGIGKFVKDYGYVWDTYDNYFCISQWYLR  
RISENINKLRLGCNWQFIPVDEGWTE\*\*

FIGURE 11

**A: BoNTA(H<sub>N</sub>) synthetic gene SEQ ID NO: 19**

atgGCTCTGAACGACCTGTGCATCAAAGTTAACAACCTGGGACCTGTTCTTC  
TCCCCGTCTGAAGACAACTTCACTAACGACCTGAACAAAGGCGAAGAAA  
TCACCTCCGACACTAACATCGAAGCTGCTGAAGAAAACATCTCTCTGGA  
CCTGATCCAGCAGTACTACCTGACTTTCAACTTCGACAACGAACCGGAA  
AACATCTCCATCGAAAACCTGTCTTCCGACATCATCGGTCAGCTGGAAC  
GATGCCGAACATCGAACGCTTCCCGAACGGCAAGAAATACGAACTGGAC  
AAATACACCATGTTCCACTACCTGCGTGCTCAGGAATTCGAACACGGTA  
AATCTCGTATCGCTCTGACTAACTCCGTTAACGAAGCTCTGCTGAACCCG  
TCTCGCGTTTACACCTTCTTCTTCCGACTACGTTAAGAAAGTTAACAA  
AGCTACTGAAGCTGCTATGTTCCCTGGGTTGGGTTGAACAGCTGGTTTACG  
ACTTCACCGACGAAACTTCTGAAGTTTCCACCACTGACAAAATCGCTGAC  
ATCACTATCATCATCCCGTACATCGGCCCGGCTCTGAACATCGGTAACAT  
GCTGTACAAAGACGACTTCGTTGGTGCTCTGATCTTCTCTGGCGCTGTTA  
TCCTGCTGGAATTCATCCCGGAAATCGCTATCCCGGTTCTGGGTACCTTC  
GCTCTGGTTTCTACATCGCTAACAAAGTTCTGACTGTTTCAGACCATCGA  
CAACGCTCTGTCTAAACGTAACGAAAAATGGGACGAAGTTTACAAATAC  
ATCGTTACTAACTGGCTGGCTAAAGTTAACACTCAGATCGACCTGATCCG  
TAAGAAGATGAAAGAAGCTCTGGAAAACCAGGCTGAAGCTACTAAAGC  
TATCATCAACTACCAGTACAACCAGTACACCGAAGAAGAAAAGAACAAC  
ATCAACTTCAACATCGATGACCTGTCCTCTAAACTGAACGAATCCATCAA  
CAAAGCTATGATCAACATCAACAAATTCCTGAACCAGTGCTCTGTTTCCT  
ACCTGATGAACTCTATGATCCCGTACGGCGTTAAACGCCTGGAAGACTTC  
GACGCTTCCCTGAAAGACGCTCTGCTGAAATACATCCGTGACAACTACG  
GTACTCTGATCGGCCAGGTTGACCGTCTGAAAGACAAGGTTAACAAACAC  
CCTGTCTACTGACATCCCGTTCCAGCTGTCCAAATACGTTGACAACCAGta  
a

**B: BoNTA(H<sub>N</sub>) encoded protein SEQ ID NO: 20**

MALNDLCIKVNNWDLFFSPSEDNFTNDLNKGEEITSDTNIEAAEENISLDLIQ  
QYYLTFNFDNEPENISIENLSSDIIGQLELMPNIERFPNGKKYELDKYTMFHY  
LRAQEFEHGKSRIALTNSVNEALLNPSRVYTFSSDYVKKVKNKATEAAMFL  
GWVEQLVYDFTDETSEVSTTDKIADITHIIPYIGPALNIGNMLYKDDFVGALIF  
SGAVILLEFIPEIAIPVLGTFALVSYANKVLTQVQIDNALSKEKWEDEVYK  
YIVTNWLAKVNTQIDLIRKKMKEALENQAEATKAIINYQYNQYTEEEKNNI  
NFNIDDLSSKLNESINKAMININKFLNQCSVYLMNSMIPYGVKRLEDFFDASL  
KDALLKYIRDNYGTLIGQVDRLKDKVNNTLSTDIPFQLSKYVDNQ\*

FIGURE 12

**A: BoNTB(H<sub>N</sub>) synthetic gene SEQ ID NO: 21**

atgGCTCCAGGAATCTGTATCGACGTCGACAACGAGGACTTGTTCTTCATC  
GCTGACAAGAACTCCTTCTCCGACGACTTGTCCAAGAACGAGAGAATCG  
AGTACAACACCCAGTCCAACATCATCGAGAACGACTTCCCAATCAACGA  
GTTGATCTTGGACACCGACTTGATCTCCAAGATCGAGTTGCCATCCGAGA  
ACACCGAGTCCTTGACTGACTTCAACGTCGACGTCCCAGTCTACGAGAA  
GCAACCAGCTATCAAGAAGATTTTCACCGACGAGAACACCATCTTCCAA  
TACCTGTACTCTCAGACCTTCCCTTTGGACATCAGAGACATCTCCTTGAC  
CTCTTCCCTTCGACGACGCCCTGCTGTTCTCCAACAAGGTCTACTCCTTCT  
CTCCATGGACTACATCAAGACTGCTAACAAGGTCGTCGAGGGCCGGTTTG  
TTCGCTGGTTGGGTCAAGCAGATCGTCAACGATTTTCGTCATCGAGGCTAA  
CAAGTCCAACACCATGGACAAGATTGCCGACATCTCCTTGATTGTCCCAT  
ACATCGGTTTGGCCTTGAACGTCGGTAACGAGACCGCCAAGGGTAACTT  
CGAGAACGCTTTTCGAGATCGCTGGTGCCTCCATCTTGTTGGAGTTCATCC  
CAGAGTTGTTGATCCCAGTCGTCGGTGCCTTCTTGTTGGAGTCTACATC  
GACAACAAGAACAAGATCATCAAGACCATCGACAACGCTTTGACCAAGA  
GAAACGAGAAGTGGTCCGACATGTACGGTTTGATCGTCGCCCAATGGTT  
GTCCACCGTCAACACCCAATTCTACACCATCAAGGAGGGTATGTACAAG  
GCCTTGAACCTACCAGGCCCAAGCTTTGGAGGAGATCATCAAGTACAGAT  
ACAACATCTACTCCGAGAAGGAGAAGTCCAACATTAACATCGACTTCAA  
CGACATCAACTCCAAGCTGAACGAGGGTATTAACCAGGCCATCGACAAC  
ATCAACAACCTTCATCAACGGTTGTTCCGTCTCCTACTTGATGAAGAAGAT  
GATTCCATTGGCCGTGCGAGAAGTTGTTGGACTTCGACAACACCCTGAAG  
AAGAACTTGTTGAACCTACATCGACGAGAACAAAGTTGACTTGATCGGTT  
CCGCTGAGTACGAGAAGTCCAAGGTCAACAAGTACTTGAAGACCATCAT  
GCCATTGACTTGTCCATCTACACCAACGACACCATCTTGATCGAGATGT  
TCtaa

**B: BoNTB(H<sub>N</sub>) encoded protein SEQ ID NO: 22**

MAPGICIDVDNEDLFFIADKNSFSDDLKNERIEYNTQSNIENDFPINELILD  
TDLISKIELPSENTESLTDFNVDVPVYEKQPAIKKIFTDENTIFQYLYSQTFPLD  
IRDISLTSSFDDALLFSNKVYSFFSMDYIKTANKVVEAGLFAGWVKQIVNDF  
VIEANKSNTMDKIADISLIVPYIGLALNVGNETAAGNFENAFEIAGASILLEFI  
PELLIPVVGAFLLSYIDNKNKIIKTIDNALTKRNEKWSDMYGLIVAQWLST  
VNTQFYTIKEGMYKALNYQAQALEEIIKYRYNIYSEKEKSNINIDFNDINSKL  
NEGINQAIDNINNFINGCSVSYLMKKMIPLAVEKLLDFDNTLKKNNLLNYIDE  
NKLYLIGSAEYEKSKVNKYLKTIMPFDLSIYTNDTILIEMF\*

FIGURE 13

**A: BoNTC<sub>1</sub>(H<sub>N</sub>) synthetic gene SEQ ID NO: 23**

atgTCCCTGTACAACAAGACCCTTGACTGTAGAGAGCTGCTGGTGAAGAA  
CACTGACCTGCCATTCATCGGTGACATCAGTGACGTGAAGACTGACATCT  
TCCTGCGTAAGGACATCAACGAGGAGACTGAGGTGATCTACTACCCAGA  
CAACGTGTGAGTAGACCAAGTGATCCTCAGTAAGAACACCTCCGAGCAT  
GGACAAGTAGACCTGCTCTACCCTAGTATCGACAGTGAGAGTGAGATCC  
TGCCAGGGGAGAATCAAGTCTTCTACGACAACCGTACCCAGAACGTGGA  
CTACCTGAACTCCTACTACTACCTAGAGTCTCAGAAGCTGAGTGACAAC  
GTGGAGGACTTCACCTTTCACGCGTTCAATCGAGGAGGCTCTGGACAACA  
GTGCAAAGGTGTACACTTACTTCCCTACCCTGGCTAACAAGGTGAATGCC  
GGTGTGCAAGGTGGTCTGTTCCCTGATGTGGGCAAACGACGTGGTTGAGG  
ACTTCACTACCAACATCCTGCGTAAGGACACACTGGACAAGATCTCAGA  
TGTGTCAGCTATCATCCCCTACATCGGACCCGCACTGAACATCTCCAACT  
CTGTGCGTCGTGGAAACTTCACTGAGGCATTCGCAGTCACTGGTGTCAACC  
ATCCTGCTGGAGGCATTCCCTGAGTTCACAATCCCTGCTCTGGGTGCATT  
CGTGATCTACAGTAAGGTCCAGGAGCGAAACGAGATCATCAAGACCATC  
GACAAGTGTCTGGAGCAGAGGATCAAGAGATGGAAGGACTCCTACGAGT  
GGATGATGGGAACGTGGTTGTCCAGGATCATCACCCAGTTCAACAACAT  
CTCCTACCAGATGTACGACTCCCTGAACTACCAGGCAGGTGCAATCAAG  
GCTAAGATCGACCTGGAGTACAAGAAGTACTCCGGAAGCGACAAGGAG  
AACATCAAGAGCCAGGTTGAGAACCTGAAGAACAGTCTGGACGTCAAG  
ATCTCGGAGGCAATGAACAACATCAACAAGTTCATCCGAGAGTGCTCCG  
TCACCTACCTGTTCAAGAACATGCTGCCTAAGGTCATCGACGAGCTGAA  
CGAGTTCGACCGAAACACCAAGGCAAAGCTGATCAACCTGATCGACTCC  
CATAACATCATCCTGGTTCGGTGAGGTCGACAAGCTGAAGGCAAAGGTAA  
ACAACAGCTTCCAGAACtaa

**B: BoNTC<sub>1</sub>(H<sub>N</sub>) encoded protein SEQ ID NO: 24**

MSLYNKTLDCRELLVKNTDLPFIGDISDVKTDIFLRKDINEETEVIYYPDNVS  
VDQVILSKNTSEHGQLDLLYPSIDSESEILPGENQVFYDNRTQNVLDYLSYY  
YLESQKLSDNVEDFTFTRSIEEALDNSAKVYTYFPTLANKVNAGVQGGFL  
MWANDVVEDFTTNILRKDTLDKISDVSAIIPYIGPALNISNSVRRGNFTEAFA  
VTGVTTILLEAFPEFTIPALGAFVIYSKVQERNEIIKTIDNCLEQRIKRWKDSYE  
WMMGTWLSRIITQFNISYQMYDSLNYQAGAIKAKIDLEYKKYSGSDKENI  
KSQVENLKNSLDVKISEAMNNINKFIRECSVTYLFKNMLPKVIDELNEFDRN  
TKAKLINLIDSHNILLVGEVDKLKAKVNNSFQN\*

FIGURE 14

**A: BoNTD(H<sub>N</sub>) synthetic gene SEQ ID NO: 25**

atggccAACTCCCGTGACGACTCCACCTGCATCAAGGTCAAGAACAAACAGA  
CTGCCATACGTTGCCGACAAGGACTCCATCTCCCAGGAGATCTTCGAGA  
ACAAGATCATCACCGACGAGACCAACGTTCAAAACTACTCCGACAAGTT  
CTCTTTGGACGAGTCCATCCTGGACGGTCAGGTCCCAATCAACCCAGAG  
ATCGTCGACCCACTGTTGCCAAACGTCAACATGGAGCCATTGAACTTGCC  
AGGTGAGGAGATCGTCTTCTACGACGACATCACCAAGTACGTCGACTAC  
TTGAACTCCTACTACTACTTGGAGTCTCAAAAGTTGTCTAACAACGTCGA  
GAACATCACCTTGACCACCTCCGTCGAGGAGGCCTTGGGTACTCTAACA  
AGATCTACACCTTCCTGCCATCCTTGGCTGAGAAGGTTAACAAGGGTGT  
CAAGCTGGTTTGTTCCTGAACTGGGCCAACGAGGTCGTCGAGGACTTCA  
CCACCAACATCATGAAGAAGGACACCCTGGACAAGATCTCCGACGTCTC  
CGTCATCATCCCATAACATCGGTCCAGCCTTGAACATCGGTAACCTCCGCCC  
TGAGAGGTAACCTCAACCAGGCCTTCGCCACCGCCGGTGTGCCTTCCTG  
CTGGAGGGTTTCCCAGAGTTCACCATCCCAGCCCTGGGTGTCTTCACCTT  
CTACTCCTCCATCCAGGAGAGAGAGAAGATCATCAAGACCATCGAGAAC  
TGCTTGGAGCAGAGAGTCAAGAGATGGAAGGACTCCTACCAGTGGATGG  
TTTCCAACCTGGCTGTCCAGAATCACCAACCAATTCAACCACATCAACTAC  
CAGATGTACGACTCCCTGTCCTACCAGGCCGACGCCATCAAGGCCAAGA  
TCGACCTGGAGTACAAGAAGTACTCCGGTTCCGACAAGGAGAACATCAA  
GTCCCAGGTCGAGAACCTGAAGAAGTCTTGGACGTCAAGATCTCCGAG  
GCCATGAACAACATCAACAAGTTCATCCGTGAGTGTTCGTCACCTACCT  
GTTCAAGAACATGCTGCCAAAGGTCATCGACGAGCTGAACAAGTTCGAC  
CTGAGAACCAAGACCGAGCTGATCAACCTGATCGACTCCCAACATCA  
TCCTGGTTGGTGAGGTTGACtaa

**B: BoNTD(H<sub>N</sub>) encoded protein SEQ ID NO: 26**

MANSRDDSTCIKVKNNRLPYVADKDSISQEIFENKIITDETNVQNYSDKFSLD  
ESILDGQVPINPEIVDPLLPNVNMEPLNLPGEIIVFYDDITKYVDYLNSYYL  
ESQKLSNNVENTLTTTSVEEALGYSNKIYTFLPSLAEKVNKGVQAGLFLNWA  
NEVEDFTTNIMKKDTLDKISDVSIIPIYGPALNIGNSALRGNFNQAFATAG  
VAFLEGFPEFTIPALGVFTFYSSIQEREKIITIENTCLEQRVKRWKDSYQWM  
VSNWLSRITTQFNHINYQMYDSLSYQADAIKAKIDLEYKKYSGSDKENIKSQ  
VENLKNSLDVKISEAMNNINKFIRECSVTYLFKNMLPKVIDELNKFDLRTKT  
ELINLIDSHNIILVGEVD\*

FIGURE 15

**A: BoNTE(H<sub>N</sub>) synthetic gene SEQ ID NO: 27**

atgTCCATCTGCATCGAGATCAACAACGGTGAGCTGTTCTTCGTGGCTTCC  
GAGAACAGTTACAACGATGACAACATCAACACTCCTAAGGAGATTGACG  
ACACCGTCACTTCTAACAACAACCTACGAAAACGACCTGGACCAGGTCAT  
CCTAAACTTCAACTCCGAGTCCGCCCTGGTCTGTCCGACGAGAAGCTGA  
ACCTGACCATCCAGAACGACGCTTACATCCCAAAGTACGACTCCAACGG  
TACATCCGATATCGAGCAGCATGACGTTAACGAGCTTAACGTCTTCTTCT  
ACTTAGACGCTCAGAAGGTGCCCGAGGGTGAGAACAACGTCAATCTCAC  
CTCTTCAATTGACACAGCCTTGTGGAGCAGCCTAAGATCTACACCTTCT  
TCTCCTCCGAGTTCATCAACAACGTCAACAAGCCTGTGCAGGCCGCATTG  
TTCGTAAGCTGGATTCAGCAGGTGTTAGTAGACTTCACTACTGAGGCTAA  
CCAGAAGTCCACTGTTGACAAGATCGCTGACATCTCCATCGTCGTCCCAT  
ACATCGGTCTGGCTCTGAACATCGGCAACGAGGCACAGAAGGGCAACTT  
CAAGGATGCCCTTGAGTTGTTGGGTGCCGGTATTTTGTGGAGTTCGAAC  
CCGAGCTGCTGATCCCTACCATCCTGGTCTTCACGATCAAGTCCTTCCTG  
GGTTCCTCCGACAACAAGAACAAGGTCATTAAGGCCATCAACAACGCCC  
TGAAGGAGCGTGACGAGAAGTGGAAGGAAGTCTATTCTTCATCGTCTC  
GAACTGGATGACCAAGATCAACACCCAGTTCAACAAGCGAAAGGAGCA  
GATGTACCAGGCTCTGCAGAACCAGGTCAACGCCATCAAGACCATCATC  
GAGTCCAAGTACAACCTCTACACCTGGAGGAGAAGAACGAGCTTACCA  
ACAAGTACGATATCAAGCAGATCGAGAACGAGCTGAACCAGAAGGTCTC  
CATCGCCATGAACAACATCGACAGGTTCTTGACCGAGTCCTCCATCTCCT  
ACCTGATGAAGCTCATCAACGAGGTCAAGATCAACAAGCTGCGAGAGTA  
CGACGAGAATGTCAAGACGTACCTGCTGAACTACATCATCCAGCACGGA  
TCCATCCTGtaa

**B: BoNTE(H<sub>N</sub>) encoded protein SEQ ID NO: 28**

MSICIEINNGELFFVASSENSYNDDNINTPKEIDDTVTSNNNYENDLDQVILNF  
NSESAPGLSDEKLNLTIQNDA YIPKYDSNGTSDIEQHDVNELNVFFYLDAQK  
VPEGENNVNLTSSIDTALLEQPKIYTFFSSEFINNVNKPVQAALFVSWIQQVL  
VDFTTEANQKSTVDKIADISIVVPYIGLALNIGNEAQKGNFKDALELLGAGIL  
LEFEPELLIPTILVFTIKSFLGSSDNKNKVIKAINNALKERDEKWKEVYSFIVS  
NWMTKINTQFNKRKEQMYQALQNQVNAIKTIIESKYSYTLLEKNELTNKY  
DIKQIENELNQKVSIAMNNIDRFLTESISYLMKLINEVKINKLREYDENVKT  
YLLNYIIQHGSIL\*

FIGURE 16

**A: BoNTF(H<sub>N</sub>) synthetic gene SEQ ID NO: 29**

atgGCCCCACCACTGTGTATTAGAGTCAACAACCTCAGAATTATTCTTT  
GTCGCTTCCGAGTCAAGCTACAACGAGAACGATATTAACACACCTAAAG  
AGATTGACGATACTACCAACCTAAACAACAACCTACCGGAACAACCTGGA  
TGAGGTTATTTTGGATTACAACCTCACAGACCATCCCTCAAATTTCCAACC  
GTACCTTAAACACTCTTGTCCAAGACAACCTCCTACGTTCCAAGATACGAT  
TCTAACGGTACCTCAGAGATCGAGGAGTATGATGTTGTTGACTTTAACGT  
CTTTTTCTATTTGCATGCCCAGAAGGTGCCAGAAGGTGAAACCAACATCT  
CATTGACTTCTTCCATTGATACCGCCTTGTGGAAGAGTCCAAGGATATC  
TTCTTTTCTTCGGAGTTTATCGATACTATCAACAAGCCTGTCAACGCCGC  
TCTGTTCAATTGATTGGATTAGCAAGGTCATCAGAGATTTTACCACTGAAG  
CTACTCAAAAGTCCACTGTTGATAAGATTGCTGACATCTCTTTGATTGTC  
CCCTATGTCCGGTCTTGCTTTGAACATCATTATTGAGGCAGAAAAGGGTAA  
CTTTGAGGAGGCTTTTGAATTGTTGGGAGTTGGTATTTTGTGAGTTTG  
TTCCAGAACTTACCATTCTGTCATTTTAGTTTTTACGATCAAGTCCTACA  
TCGATTCATACGAGAACAAGAATAAAGCAATTAAGCTATTAACAACCTC  
CTTGATCGAAAGAGAGGCTAAGTGGAAGGAAATCTACTCATGGATTGTA  
TCAAACCTGGCTTACTAGAATTAACACTCAATTTAACAAGAGAAAGGAGC  
AAATGTACCAGGCTCTGCAAAACCAAGTCGATGCTATCAAGACTGCAAT  
TGAATACAAGTACAACAACCTATACTTCCGATGAGAAGAACAGACTTGAA  
TCTGAATACAATATCAACAACATTGAAGAAGAGTTGAACAAGAAAGTTT  
CTTTGGCTATGAAGAATATCGAAAGATTTATGACCGAATCCTCTATCTCT  
TACTTGATGAAGTTGATCAATGAGGCCAAGGTTGGTAAGTTGAAGAAGT  
ACGATAACCACGTTAAGAGCGATCTGCTGAACCTACATTCTCGACCACAG  
ATCAATCCTGGGAGAGCAGACAAACGAGCTGAGTGATTTGGTTACTTCC  
ACTTTGAACTCCTCCATTCCATTTGAGCTTTCT<sub>taa</sub>

**B: BoNTF(H<sub>N</sub>) encoded protein SEQ ID NO: 30**

MAPPRLCIRVNNSSELFVASESSYNENDINTPKEIDDTTNLNNNYRNNLDEVI  
LDYNSQTIPQISNRTLNTLVQDNSYVPRYDSNGTSEIEEYDVVDFNVFFYLH  
AQKVPEGETNISLTSSIDTALLEESKDIFFSSEFIDTINKPVNAALFIDWISKVIR  
DFTTEATQKSTVDKIADISLIVPYVGLALNIIIEAEKGNFEEAFELLGVGILLEF  
VPELTIPVILVFTIKSYIDSYENKNKAIAKAINNSLIEREAKWKEIYSWIVSNWL  
TRINTQFNKRKEQMYQALQNQVDAIKTAIEYKYNNYTSDEKNRLESEYNIN  
NIEEELNKKVSLAMKNIERFMTESISYLMKLINEAKVGKLKKYDNHVKSDL  
LNYILDHRSILGEQTNELSDLVTSTLNSSIPFELS\*



FIGURE 17

**A: BoNTG(H<sub>N</sub>) synthetic gene SEQ ID NO: 31**

atggccAAAAATACCGGTAAATCTGAACAGTGTATTATTGTTAATAATGAG  
GATTTATTTTTTCATAGCTAATAAAGATAGTTTTTCAAAGATTAGCTAA  
AGCAGAACTATAGCATATAATACACAAAATAATACTATAGAAAATAAT  
TTTTCTATAGATCAGTTGATTTTAGATAATGATTTAAGCAGTGGCATAGA  
CTTACCAAATGAAAACACAGAACCATTTACAAATTTTGACGACATAGAT  
ATCCCTGTGTATATTAAACAATCTGCTTTAAAAAAAATTTTTGTGGATGG  
AGATAGCCTTTTTGAATATTTACATGCTCAAACATTTCTTCTAATATAG  
AAAATCTACAATAACGAATTCATTAAATGATGCTTTAAGAAATAATAA  
TAAAGTCTATACTTTTTTTCTACAAACCTTGTGAAAAAGCTAATACAG  
TTGTAGGTGCTTCACTTTTTGTAACTGGGTAAAAGGAGTAATAGATGAT  
TTTACATCTGAATCCACACAAAAAGTACTATAGATAAAGTTTCAGATGT  
ATCCATAATTATCCCTATATAGGACCTGCTTTGAATGTAGGAAATGAAA  
CAGCTAAAGAAAATTTTAAAAATGCTTTTGAAATAGGTGGAGCCGCTAT  
CTTAATGGAGTTTATTCAGAACTTATTGTACCTATAGTTGGATTTTTTAC  
ATTAGAATCATATGTAGGAAATAAAGGGCATATTATTATGACGATATCC  
AATGCTTTAAAGAAAAGGGATCAAAAATGGACAGATATGTATGGTTTGA  
TAGTATCGCAGTGGCTCTCAACGGTTAATACTCAATTTTATACAATAAAA  
GAAAGAATGTACAATGCTTTAAATAATCAATCACAAGCAATAGAAAAAA  
TAATAGAAGATCAATATAATAGATATAGTGAAGAAGATAAAATGAATAT  
TAACATTGATTTTAATGATATAGATTTTAAACTTAATCAAAGTATAAATT  
TAGCAATAAACAAATATAGATGATTTTATAAACCAATGTTCTATATCATAT  
CTAATGAATAGAATGATTCCATTAGCTGTAAAAAAGTTAAAAGACTTTG  
ATGATAATCTTAAGAGAGATTTATTGGAGTATATAGATACAAATGAACT  
ATATTTACTTGATGAAGTAAATATTCTAAAATCAAAGTAAATAGACAC  
CTAAAAGACAGTATACCATTTGATCTTTCACTATATACCTaa

**B: BoNTG(H<sub>N</sub>) encoded protein SEQ ID NO: 32**

MAKNTGKSEQCIIVNNEDLFFIANKDSFSKDLAKAETIA YNTQNNTIENNFSI  
DQLILDNDLSSGIDLPNENTEPFTNFDDIDIPVYIKQSALKKIFVDGDSLFEYL  
HAQTFPSNIENLQLTNSLNDALRNNNKVYTFSTNLVEKANTVVGASLFVN  
WVKGVIDDFTSESTQKSTIDKVS DVSIIPYIGPALNVGNETAKENFKNAFEIG  
GAAILMEFIPELIVPIVGFFTLESYVGNKGHIIMTISNALKKRDQKWTD MYGL  
IVSQWLSTVNTQFYTIKERMYNALNNQSQAIEKIIDQYNRYSEEDKMNINI  
DFNDIDFKLNQSINLAINNIDDFINQCSISYLMNRMIPLA VKKLKDFDDNLKR  
DLLEYIDTNELYLLDEVNILKSKVNRHLKDSIPFDLSLYT\*

FIGURE 18

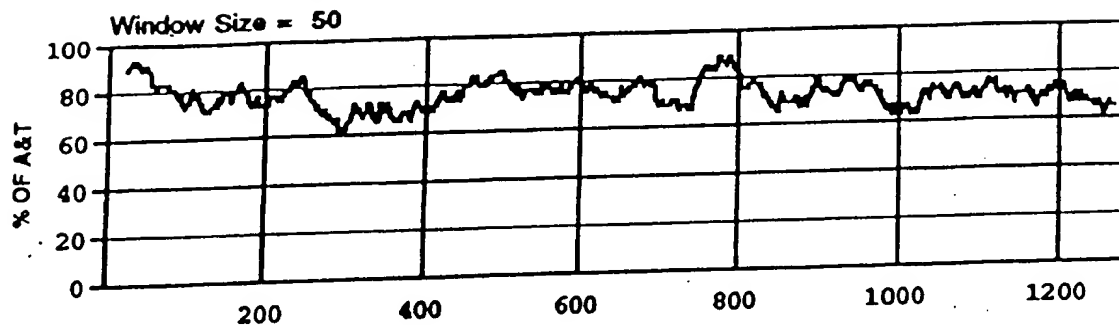
**A: First BoNTF(Hc) gene: SEQ ID NO: 33**

GAATTCACGatgTCTTACACTAACGACAAAATCCTGATCCTGTACTTCAAC  
AAACTGTACAAAAAATCAAAGACAACCTCTATCCTGGACATGCGTTACG  
AAAACAACAAATTCATCGACATCTCTGGCTATGGTTCTAACATCTCTATC  
AACGGTGACGTCTACATCTACTCTACTAACCAGCAACCAGTTCCGGTATCTA  
CTCTTCTAAACCGTCTGAAGTAAACATCGCTCAGAACAACGACATCATCT  
ACAACGGTCGTTACCAGAACTTCTCTATCTCTTTCTGGGTTTCGTATCCCG  
AAATACTTCAACAAAGTTAACCTGAACAACGAATACACTATCATCGACT  
GCATCCGTAACAACAACCTCTGGTTGGAAAATCTCTCTGAACTACAACAA  
AATCATCTGGACTCTGCAGGACACTGCTGGTAACAACCAGAACTGGTT  
TTCAACTACACTCAGATGATCTCTATCTCTGACTACATTAATAAATGGAT  
CTTCGTTACTATCACTAACAACCGTCTGGGTAACCTCTCGTATCTACATCA  
ACGGTAACCTGATCGATGAAAAATCTATCTCTAACCTGGGTGACATCCA  
CGTTTCTGACAACATCCTGTTCAAAATCGTTGGTTGCAACGACACGCGTT  
ACGTTGGTATCCGTTACTTCAAAGTTTTTCGACACTGAACTGGGTAAAAC  
GAAATCGAACTCTGTACTCTGACGAACCGGACCCGTCTATCCTGAAAG  
ACTTCTGGGGTAACTACCTGCTGTACAACAACGTTACTACCTGCTGAAC  
CTGCTCCGGACTGACAAATCTATCACTCAGAACTCTAACTTCCTGAACAT  
CAACCAGCAGCGTGGTGTATTATCAGAAACCTAATATCTTCTCTAACTC  
GTCTGTACACTGGTGTGGAAGTTATCATCCGTAAAAACGGTTCTACTGAC  
ATCTCTAACTGACAACTTCGTACGTAAAAACGACCTGGCTTACATCAA  
CGTTGTTGACCGTGACGTTGAATACCGTCTGTACGCTGACATCTCTATCG  
CTAAACCGGAAAAAATCATCAAACTGATCCGTACTTCTAACTCTAACAA  
CTCTCTGGGTCAGATCATCGTTATGGACTCGATCGGTAACAACCTGCACTA  
TGAACCTCCAGAACAAACCGGTGGTAACATCGGTCTGCTGGGTTTCCA  
CTCTAACAACTGGTTGCTTCTTCATGGTACTACAACAACATCCGTAAAA  
ACACTTCTTCTAACGGTTGCTTCTGGTCTTTCATCTCTAAAGAACACGGTT  
GGCAGGAAAACtaaGAATTC

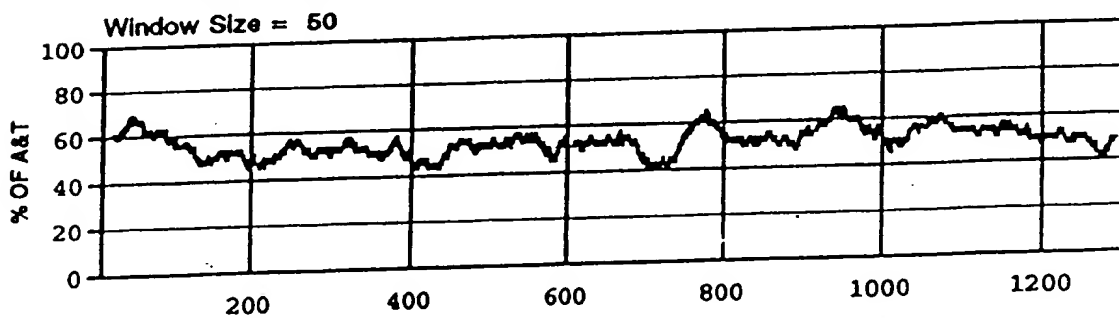
**B: BoNTF(Hc) #1 encoded protein: SEQ ID NO: 34**

MSYTNDKILILYFNKLYKKIKDNSILDMRYENNKFIDISGYGSNISINGDVYIY  
STNRNQFGIYSSKPSEVNIAQNNDIIYNGRYQNFSISFWVRIPKYFNKVNLNN  
EYTIIDCIRNNNSGWKISLNYNKIIWTLQDTAGNNQKLVFNQYTMISISDYIN  
KWIFVTITNNRLGNSRIYINGNLIDEKSISNLGDIHVSDNILFKIVGCNDTRYV  
GIRYFKVFDTELKGTEIETLYSDEPDPSILKDFWGNLYLLYNKRYLLNLLRT  
DKSITQNSNFLNINQQRGVYQKPNIFSNTRLYTGVEVIIRKNGSTDISNTDNF  
VRKNDLAYINVVDRDVEYRLYADISIAKPEKIIKLIRTSNSNNSLGQIIVMDSI  
GNNCTMNFQNNNGGNIGLLGFHSNNLVASSWYYNNIRKNTSSNGCFWSFIS  
KEHGWQEN\*

### A: Natural BoNTF(Hc) Gene



### B: First BoNTF(Hc) Synthetic Gene



### C: Second BoNTF(Hc) Synthetic Gene

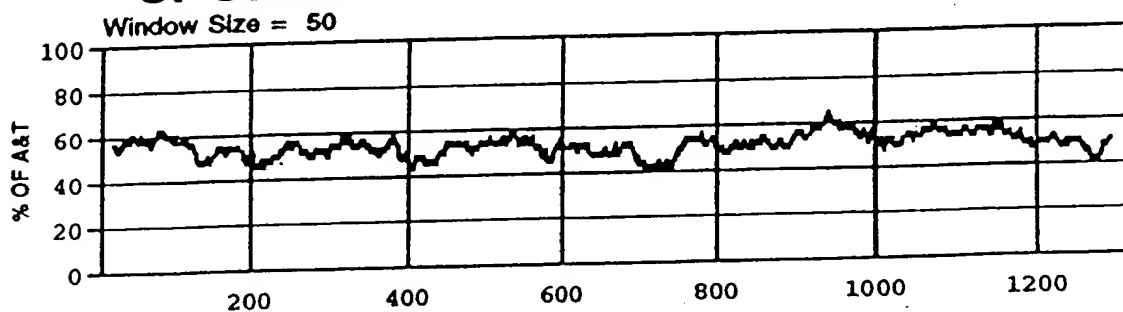
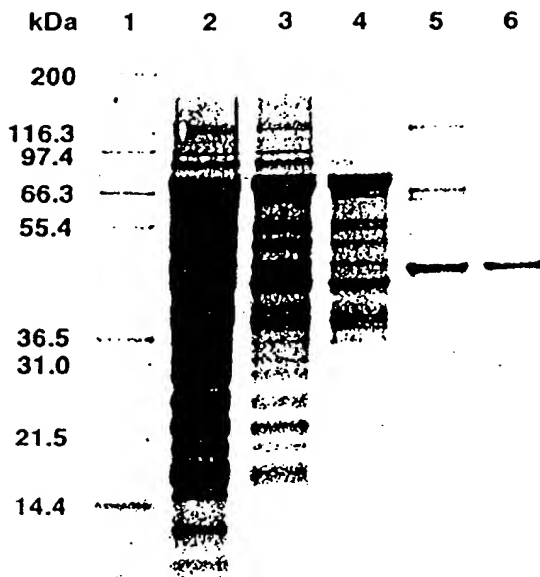


Fig 19

0910106.072001

A



B

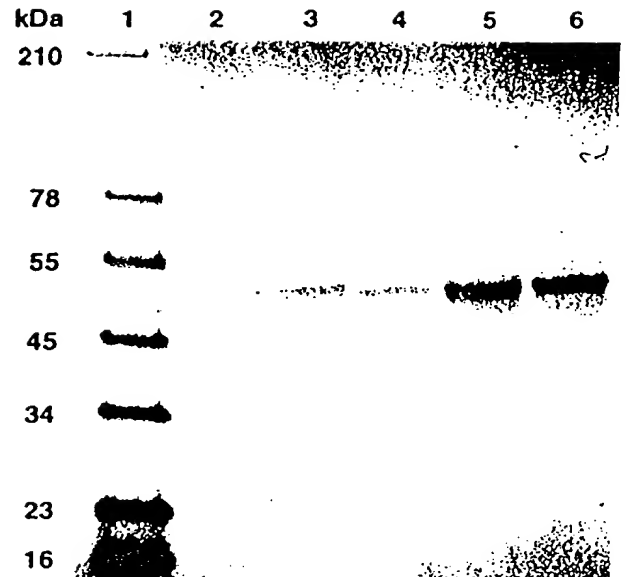


Fig 20

100220 98101660

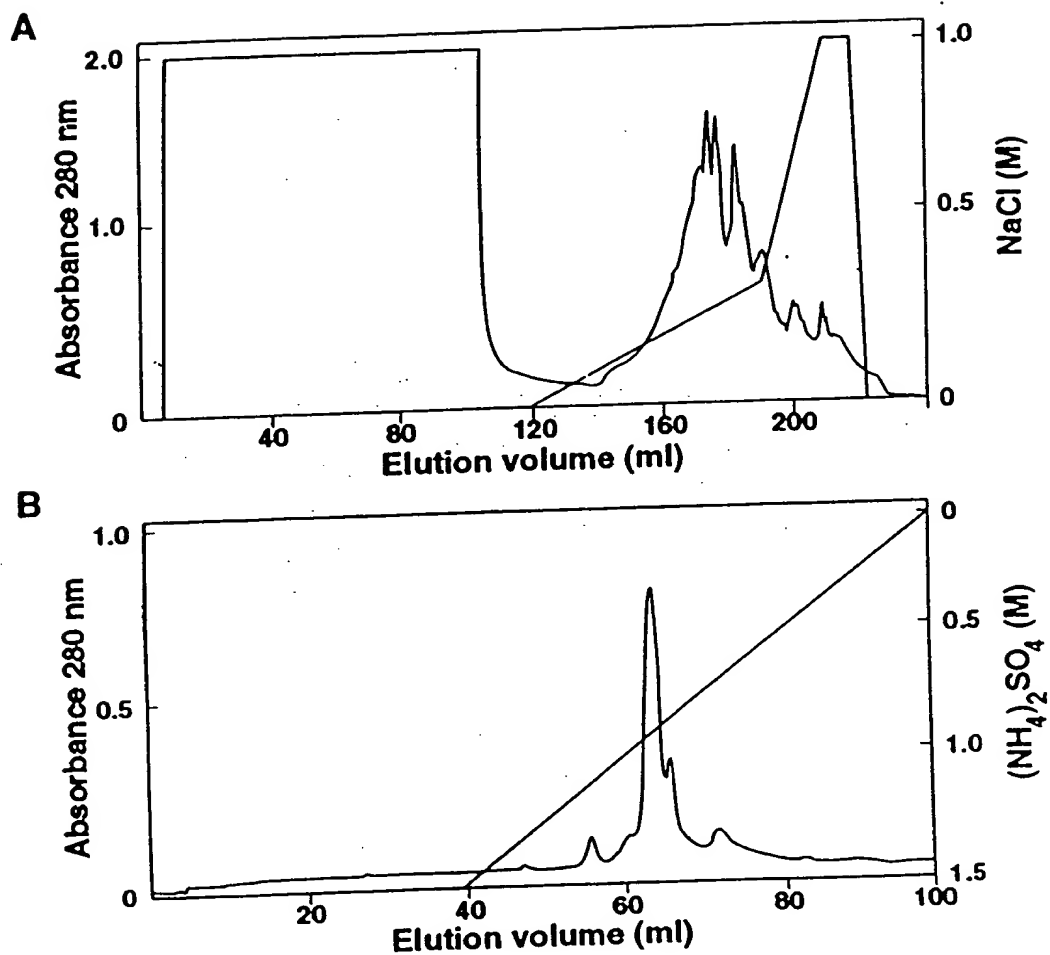


Fig 21

00010185 072001  
T00220" 98T0T600

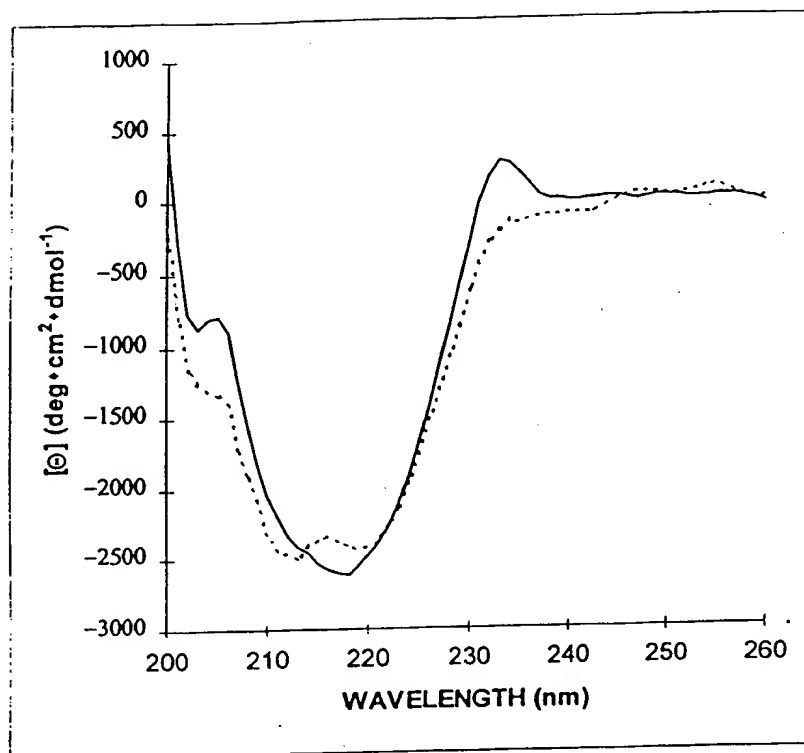


Fig 22